Response

Mangano correctly notes that the dose–response relationships in our analyses of cancer incidence in relation to the Three Mile Island (TMI) accident (*1*) are supralinear. The goodness of fit statistics would have been larger (and corresponding *p*-values smaller) had we fit regression models using the log of dose.

The substantive issue raised by Mangano, however, concerns mechanisms that could account for a larger carcinogenic effect of radiation per dose unit at low levels than at higher levels. There are three important questions regarding Mangano's interpretation: 1) Do the cancer incidence patterns reflect low dose radiation? 2) Is the study design appropriate for distinguishing the shape of radiation dose–response relationships at low levels? and 3) Is the original scaling (vs. magnitude) of dose estimates correct? We answer no to the first two questions and discussed reasons for uncertainty regarding the third in our paper (*1*).

We noted that patterns of cancer incidence were consistent with reports suggesting high doses of radiation. The appearance of large elevations in lung cancer incidence within 7 years of exposure is not consistent with previous studies of low-level radiation, where low might be defined as doses below the annual occupational limit of 50 mSv. Lung cancer elevations seen at TMI are much larger and appear with shorter latency than do elevations for workers with cumulative lung doses that are substantially above 50 mSv (*2–4*).

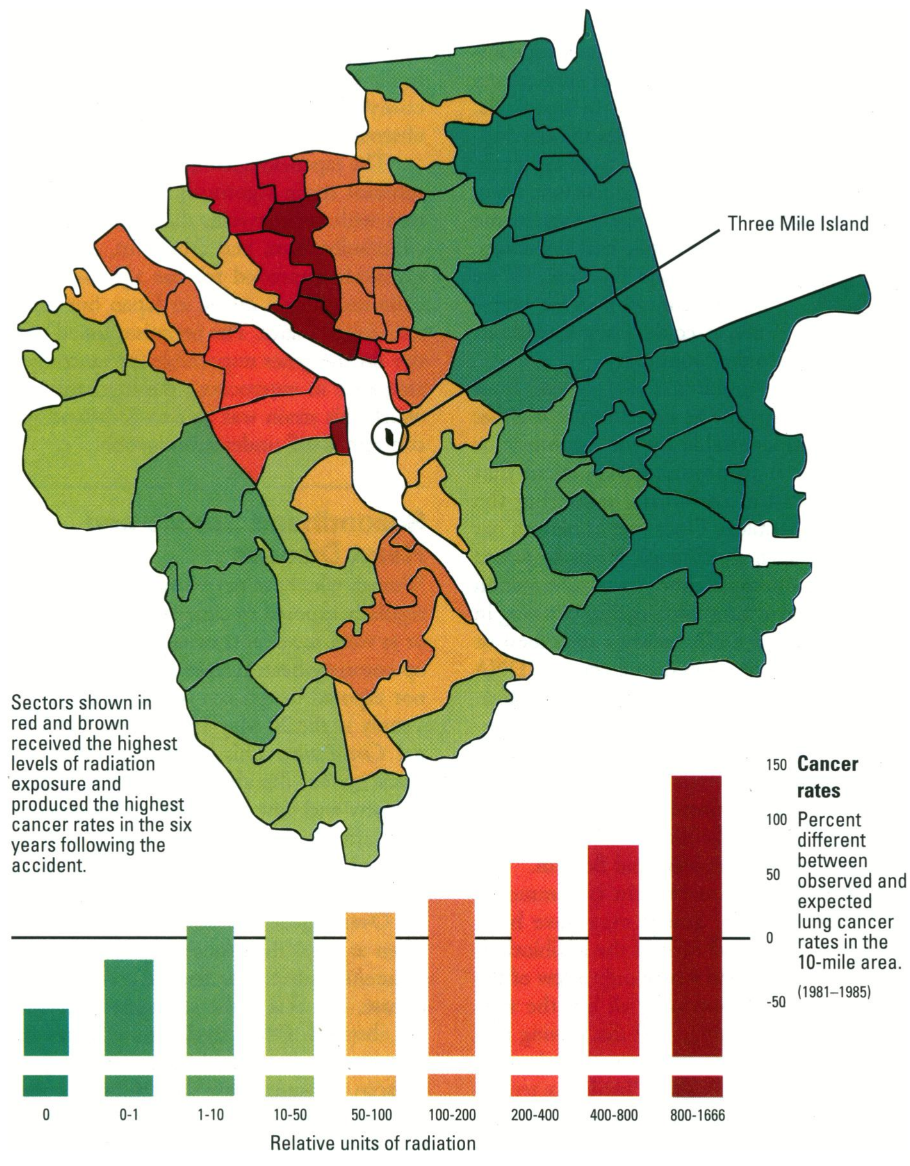

Figure 1. Three Mile Island postaccident lung cancer rates for 1981–1985 (adjusted for age, sex, and preaccident incidence) in relation to the estimated distribution of radioactive emissions from the accident. Reprinted with permission from *Endeavors* (*5*).
Credit: Julia Bryan

Furthermore, the design of the TMI study is not well suited to distinguishing between shapes of dose–response associations. Such questions would be better addressed using epidemiological designs that include radiation dose measurements for individuals rather than estimates of average doses for geographic areas, within which there is heterogeneity of individual dose. Individual dose estimates should ideally include evaluation of both external penetrating radiation and internal exposures to β- and α–emitting radionuclides, where relevant.

Subsequent to publication of our study, the lung cancer results reanalyzed by Mangano have been mapped for an article in the University of North Carolina's *Endeavors* magazine (*5*). Figure 1, which links the TMI postaccident lung cancer rates for 1981–1985 (adjusted for age, sex, and preaccident incidence) to a map of the estimated distribution of radioactive emissions from the accident, demonstrates Mangano's point that the dose response would be fairly linear on a log scale (note that the vertical axis is not on a log scale). Figure 1 also shows the large magnitude of the elevation when comparing the lowest and highest dose study areas. Given the uncertainty of dose estimates, heterogeneity within study blocks, and other limitations of study design, we caution against overinterpreting these findings in terms of low-level radiation's biological mechanisms.

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